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Treatment of Anthrax with Large Doses of Specific Serum.

by L. I. Cherevuchkina

Odeskiy Medichniy Zhurnal. 3-5: 295-300: 1930.

Anthrax is a constant guest of our Union. A timely prophylaxis of cattle and an energetic treatment of cattle and humans would have increased our agriculture and curtailed to a minimum the death rate among humans.

The wave of anthrax sicknesses, according to the data of the 1st Soviet People's Hospital (1st SPH), rises in the month of June, attains a maximum in August, September, sometimes in October and drops sharply in November. In the other months the sicknesses are counted in units.

Months	1926	1927	1928	1929
Jan	3	1	2	2
Feb	3	3	-	2
Mar	-	1	1	3
Apr	-	-	2	2
May	5	2	2	1
June	-	5	5	6
July	3	4	8	11
Aug	5	4	20	29
Sept	11	10	8	10
Oct	7	5	13	6
Nov	-	2	1	-
Dec	2	5	2	-
Total	39	42	64	72

The number of patients, calling for assistance at the 1st SPH, grows with each year and attains a rather high figure. Whereas in 1926, 39 patients passed through the 2nd isolation barracks of our hospital, in 1927 there were 42, in 1928 - 64, and in 1929 prior to the end of October the number of patients reached 72. One should note that the sicknesses of a professional nature are counted in units; the patients, in the great majority, are patients from the surrounding district and practically every one of those who became ill had suffered a cattle plague, or the patient had taken part in processing the carcasses of animals that had died at a neighboring house.

Concerning the gravity of the disease, that portion of the mild cases not requiring any treatment other than antiseptic dressings and isolation, or those who received serum one time, amounts to somewhat more than one-third of the patients; such cases in 1928 amounted to 35 %, in the same year, the cases of medium gravity amounted to 40.6 %; and last, the serious cases came to 23 %, out of which anthrax spores were bacteriologically detected in the blood of one-third. The death rate from anthrax in 1927, when we used the usual method of treatment with specific serum in small doses, from 40 cm³ to 100 cm³, equalled 9.5 %; moreover, the presence of anthrax spores in the blood of all the fatalities was ascertained. All 4 cases of sepsis died. One of these patients developed a rather satisfactory condition, but in his case sepsis developed very quickly and the commonly employed serum dose, 80 cm³ in this case, gave no result whatsoever.

In 1928 the death rate sharply drops to 3.1 %, and of the 5 patients in a state of sepsis, we lost only one (one case is not included in the computation because he did not survive 24 hours), three of the patients completely recovered. In all these cases we employed massive doses of anti-anthrax serum, which exceeded 800 cm³ in three cases. In 1929 (prior to the end of October) 2 of the three sepsis cases died (one died in the first 24 hours), one died on the fifth day and one recovered. The death rate in this instance equals 2.75 %.

Year	All Patients	Died	Death Rate %
1927	42	4	9.5
1928	64	2	3.1
1929	72	2	2.7

In order to avoid repetition we will not remain too long on the literary data and history of using antianthrax serum with humans for therapeutic purposes; they are excellently developed by Skrotskiy (Sovremennaya Meditsina. Aug-Oct 1924), and also presented in detail by Padalka (Vrachebnoe Delo No. 22, 1923). Let us only say that after Sclavo in Italy and Mendez'a in Argentina in 1897-1898, this serum was also repeatedly employed by other clinical physicians (Sobernheim, Bandi) with the same success. We in the Soviet Union, in spite of a rather large number of anthrax occurrences, much more frequently use salvarsan preparations. Serum is either not used completely, or it is employed in doses entirely insufficient for the serious cases. In addition, one should note the comparatively small number of patients for which the indicated serum was used by the various authors in our Union (Padalka - 33 cases, Morozkin - 15 cases). Our experience is incomparably greater, it encompasses 115 cases of the most varied gravity of sicknesses, and we can boldly say that antianthrax serum is an effective agent in the treatment of this serious disease and only the very neglected or unusually malignant cases do not respond to its influence.

We will permit ourselves to bring forward the histories of the disease in the more demonstrative cases.

Case 1 - L. S. , age 45 years, farmer. 19 Dec 1927 - He entered the 1st SPH on the 3rd day of the disease. Two anthrax pustules on the right hand. Surrounded by vesicles. The entire area of the hand and a portion of the

antibrachium has swelled, the skin is of a blue-reddish purple color. The glands in the axillary area have become enlarged and painful. $T^{\circ} 38.3^{\circ}-39.5^{\circ}$. A little excitation. A pulse of satisfactory fullness, 120 per minute. 80 cm³ of specific serum from the Kherson Vet. Institute was intramuscularly injected. 20 Dec - Had a restless night. The swelling has spread to the upper portion of the antibrachium. The pustules are in their previous condition. The heart sounds are dull. 80 cm³ of antianthrax serum are injected intravenously; 60 cm³, intramuscularly. 21 Dec - Rigor. No appetite. A watery stool, 2 times. The edema has spread to the entire shoulder. The pulse is soft. Anthrax spores were detected in a blood culture (Odesa Bak. Institute). Specific serum was given, 120 cm³ into the vein, 130 cm³ into the muscle. Caffeine given internally. 22 Dec - Feeling better. Appetite has appeared. Edema became softer. $T^{\circ} 38^{\circ}$. A sterile blood culture. 23 Dec - Edema is noticeably decreased. Feeling quite satisfactory. The scab is drying. On the 21st day the scab falls off. On 10 Jan 1928 the patient is released, having received in all 470 cm³ of antianthrax serum.

Case 2 - Ts. K., age 32 years. Husband is engaged in sheep-raising, often drives from the village hauling sheep material, hides and wool. 30 Jan 1928 - She entered the hospital on the 4th day of the disease. On the right cheek is an anthrax carbuncle which has a nonpainful infiltrate around it. A soft edema rises on the upper portion of the face as far as the lower eyelid, drooping onto the cheek. The right palpebral fissure is constricted. The lips are swollen, particularly the right half. Breathing and swallowing are somewhat impaired. Heart sounds are dull. Pulse 120 per minute, soft. Unitary dry rales in the lungs. 40 cm³ of antianthrax serum are injected intravenously and 80 cm³ intramuscularly. 1 Feb - The edema has grown, dropping down to the middle of the breast bone. The pustule is somewhat enlarged. The pulse is soft. $T^{\circ} 39.5^{\circ}-39.2^{\circ}$. 150 cm³ of specific serum is given into the muscle. Caffeine given internally. 2 Feb - Feeling better. The edema is in its previous condition. The skin around the pustule is of a blue-reddish purple color. The scab is more pronounced. The pulse is 112 per minute, of improved fullness. $T^{\circ} 38.2^{\circ}$. 150 cm³ of specific serum are intramuscularly injected. 3 Feb - The edema noticeably decreased. Spent the night peacefully. Sleep and appetite are satisfactory. $T^{\circ} 37.5^{\circ}$. 6 Feb - Serum rash of an urticarial type appeared. Good condition. The scab begins to dry. 8 Feb - The serum rash disappeared. The scab is well loosened. 25 Feb - The scab fell off, a small ulcer remains. The patient was released for out-patient treatment, having received in all 420 cm³ of serum.

Case 3 - M. K., age 49 years, female, a peasant from the village of Bol-yayevka. 7 Aug 1928 - She was brought to the hospital on the 4th day of the disease. A scab is forming on the back surface of the right hand; around it is a large vesicle filled with a rather turbid fluid. The entire extremity is sharply swollen. The heart sounds are deadened, the pulse is soft. $T^{\circ} 38.6^{\circ}$. 60 cm³ of specific serum are injected intravenously, the same amount intramuscularly. 9 Aug - Complains of a burning sensation in the sore arm. Sleep and appetite are decreased. The right arm is acutely swollen, the skin is of a bluish-red color. The vesicle around the scab burst. $T^{\circ} 39^{\circ}$. Anthrax spores were detected in a blood culture. Injected antianthrax serum, 60 cm³ intravenously, 120 cm³ intramuscularly. 10 Aug - The edema has grown still larger. A general lethargy. Dirotic pulse. $T^{\circ} 39.1^{\circ}$. 65 cm³ of specific serum were

injected intramuscularly. 11 Aug - General and local manifestations are in their previous condition. $T^{\circ} 39.4^{\circ}$. Injected antianthrax serum, 75 cm^3 into the vein-72 cm^3 into the muscle. 12 Aug - The edema of the extremity decreased. The night was spent restlessly, but from the morning her feelings were noticeably improved. $T^{\circ} 37.2^{\circ}$. The scab is loosening. 15 Aug - Complains of an itching over the entire body. Sleeps poorly. A large, heavy urticarial type rash is on the trunk, lower and upper extremities. Satisfactory pulse. The heart sounds are dull. 17 Aug - A fresh eruption of urticaria. The scab is drying. Condition is satisfactory. 21 Aug - The scab remains. The edema of the extremity has disappeared. 23 Aug - The scab pools off. The ulcerous surface is granulated. 29 Aug - Patient is released for out-patient treatment, having received in all 542 cm^3 of specific serum.

Case 4 - M. M., age 32 years. A peasant from Poryatovka. 9 Dec 1928 - Entered the hospital on the 3rd day of the disease. A horse had died from anthrax at his establishment. On the right side of the neck is a typical anthrax pustule surrounded by a corona of vesicles. A gel-like edema encompasses the neck and falls on the breast to the third rib. The face is pale. The respiration is somewhat impaired. The heart sounds are dull. The pulse is weak. $T^{\circ} 39^{\circ}$. Antianthrax serum from the Kherson Vet. Institute is injected, 70 cm^3 intravenously, 170 cm^3 intramuscularly. Vomiting occurs during the injection of the serum. Caffeine is given internally. 10 Dec - The patient is acutely pale. Breathing is impaired. Threadlike pulse. The heart gives a thudding sound. The carbuncle is in the same condition. The surrounding skin is of a blue-reddish purple color. The edema is noticeably increased. The neck and a portion of the face are swollen. The edema has spread downwards to the navel. The condition is extremely serious. $T^{\circ} 39.3^{\circ}$. Specific serum is injected, 120 cm^3 into the vein, 180 cm^3 into the muscle. Anthrax spores are detected in a blood culture. Adrenalin given subcutaneously. 11 Dec - The patient is in a critical condition. Breathing is impaired and shallow. The edema of the face is enlarged. The edema has dropped downward to somewhat below the navel. The skin of the neck and chest is of a blue-reddish purple color. Vesicles have emerged on the right subclavian area. Pulse 120 per minute, weak filling. The heart gives heavy thudding sounds. A normal vesicular breathing in the lungs. The spleen is not enlarged. $T^{\circ} 39.3^{\circ}$. Anthrax spores are again detected in a blood culture. Specific serum is injected, 150 cm^3 into the vein, 170 cm^3 into the muscle. 12 Dec - The patient's condition remains critical, but breathing and swallowing are freer. A weak filling pulse at 120 per minute. The swelling on the face has included the lower right eyelid. The edema has extended to the inguinal areas. The blood culture is sterile. 13 Dec - The condition is noticeably improved. The breathing is free. The pulse is of satisfactory fullness, at 84 per minute. Sleep is still disturbed, appetite is sluggish. $T^{\circ} 37.7^{\circ}-39^{\circ}$. Morphine and caffeine given internally. 14 Dec - Patient feels well. The erythema on the neck and shoulder area is losing color. Suggillation and a surface necrosis are noted in the right subclavical area. A scab begins to form. $T^{\circ} 37.7^{\circ}-38^{\circ}$. 15 Dec - There is a remnant of edema on the right cheek, neck and breast. The erythema has almost disappeared. The scab loosened. Sleep and appetite are satisfactory. 19 Dec - General condition is good. The scab is a little raised. Condition is satisfactory. There is a softening on the breast in the area of the infiltrate. 25 Dec - An incision made in the chest area along the median line, about 6 cm long, an abscess beneath the skin, necrotic

films on his muscles. Liquid pus of a dirty-yellow color. In the area of the right clavicle the wound entrance was enlarged, about 5 cm² of pus drained. Dressings. 26 Jan - Patient was released as healthy, having received 860 cm³ of antianthrax serum.

Case 5 - V. G., age 41 years, peasant. Entered the hospital 8 Aug 1928 on the 4th day of the disease. There had been no cattle plague. There is a carbuncle with a distinguishing scab on the lower portion of the left forearm. Vesicle filled with sanguinolent liquid is located on the periphery of the scab. A painless edema encompasses the whole extremity and extends to the adjoining portion of the breast. The pulse is soft at 120 per minute. T° 38.5°-39.4°. Specific serum is injected, 90 cm³ into the vein and 140 cm³ into the muscle; 120 cm³ was given intramuscularly the night before. 10 Aug - The condition has worsened. The patient is lethargic. Drinks very much. No appetite. The heart sounds are dull. The pulse is soft at 124 per minute. The edema has noticeably enlarged, it encompasses the entire extremity, goes over to the lateral area of the trunk and extends to the waist. The skin of the extremities is acutely strained. The pustule is without change. The spleen is not felt. T° 38.7°-38.2°. Anthrax spores are detected in a blood culture. Injected anti-anthrax serum, 150 cm³ intravenously, 210 cm³ intramuscularly. 11 Aug - The edema is soft and extends below the waist. The pustule is surrounded by vesicles filled with a serous fluid. The pulse is soft. The appetite is poor. The tongue is furred. The condition is critical. T° 38.5°-38.7°. Anthrax spores are again detected in a blood culture. 200 cm³ of specific serum are intramuscularly injected. Coffee is given internally. 12 Aug - The edema persists, but is somewhat softer. The vesicle around the pustule is in the same condition. The heart sounds are greatly deadened. No appetite. T° 37°. Towards evening the T° rises to 38.8°, delirium occurs. Towards morning the patient dies, having received in all 910 cm³ of serum. In the blood culture taken on 12 Aug anthrax spores are detected for the third time.

Case 6 - Ya. S., age 16 years. Assisted in production of brushes. 6 July 1926 - Entered the hospital on the third day of the disease. The anthrax carbuncle is on the right cheek. A gel-like edema encompasses the entire neck, hangs down onto the breast and reaches as far as the epigastrium. There is a dense infiltrate beneath the chin. The ulcer is of small dimensions, the size of a pea. The heart sounds are dull. Pulse is 124 per minute, of a satisfactory fullness. T° 39.3°-40.3°. The first day at the hospital the patient received 100 cm³ of specific serum intravenously and the same amount intramuscularly. 7 July - Serum was once more intramuscularly injected, 240 cm³. 8 July - At night the patient had delirium, jumped out of bed, did not recognize anyone. From the morning there were weakness and nausea. The edema has lowered to the stomach. The pustule is in its previous condition. T° 39°-40°. Pulse is soft. 200 cm³ of specific serum injected intramuscularly. 9 July - The patient again spent the night restlessly, delirium. From the morning his feelings were notably improved. The scab is in the formation stage. The edema has somewhat decreased. The skin on the neck and upper portion of the chest is of a blue-red-dish purple color. The infiltrate beneath the chin persists. T° 39.4°-39.2°. 170 cm³ of specific serum are injected intramuscularly. 10 July - Spent the night well with complete consciousness. The edema has noticeably decreased. The scab is drying. The heart sounds are dull. The T° fell critically to the

norm. 12 July - The scab fell off. The patient was released to his parents for out-patient treatment, having received in all 810 cm³ of serum.

Case 7 - G. V., age 70 years, 12 Aug 1929 - Entered the hospital on the 4th day of the disease; as a result of an erroneous diagnosis she was first admitted into the erysipelatosus clinic. The next day she was transferred into the 2nd isolation barracks with a diagnosis of anthrax. A surface necrosis on the right cheek beneath the lower eyelid. On the same side, on the forehead, is a restricted necrosis without the typical carbuncle. The eye is closed by a large edema which encompasses the entire face and spreads onto the breast as far as the third rib, it also encompasses the entire head. The heart gives heavy thudding sounds. The pulse is soft and fast. A state of dejection. The tongue is dry. Breathing is difficult. T° 38.5°. Specific serum is injected, 115 cm³ into the vein, 200 cm³ into the muscle. Caffeine is given internally. 14 Aug - The general condition is slightly improved. The necrosis beneath the eye has grown noticeably to 1/2 the size of a man's palm. The surrounding skin is of a blue-reddish purple color. The edema, both on the head and the trunk, has increased and reaches as far as the waist. The pulse is soft. 15 Aug - The edema has slightly decreased. The pulse has improved. Anthrax spores are detected in a blood culture. 120 cm³ of specific serum are given intramuscularly. 16 Aug - The edema has again increased. The left eye is shut. The necrosis beneath the eye encompasses the larger portion of the cheek. Her feelings have worsened. Refuses food. 120 cm³ of serum are given intravenously; the same amount is also given intramuscularly. 17 Aug - The edema has noticeably decreased, both eyes have opened. The pulse is soft. 18 Aug - The edema is again decreased. The necrosis is beginning to separate from the healthy tissue. Much pus is released. The pulse is somewhat fast, of a satisfactory fullness and rhythmic. T° 37.9°-38°. 19 Aug - The general condition is noticeably improved. The edema of the face and head has almost disappeared, but still persists on the breast. A profuse discharge of malodorous pus. 22 Aug - The edema has almost disappeared. A profuse discharge. T° is normal. 28 Aug - The ulcerous surface on the cheek is healing. It persists on the forehead. 6 Sep - Patient is released with a small ulcerous surface, having received in all 675 cm³ of specific serum.

It is plain from the cited case histories that in all the described cases the serum was employed in massive doses, amounting to 810 cm³ in one case, 860 cm³ in another, and we have no doubt that only such a energetic treatment saved the lives of these exceptionally serious cases. Anthrax spores were detected in the patients' blood in 5 of the described cases, in the other 2 cases by the use of serum, without a doubt, we succeeded in averting septicemia with the consequential lethal result. True, in case 5 despite the massive dose of serum, we did not succeed in saving the patient, but this was exceptionally critical in virulence, a point that is evident from the fact that in spite of the huge dose of serum injected (910 cm³), anthrax spores were found in the blood three times in succession. In addition, the improvement which we considered indefinite (drop in T° to the norm, decrease of the edema) proved to be temporary; it is possible that with the use of somewhat more serum, we may have been able to save even this patient.

We did not inject more than 150 cm³ of serum into the vein at one time, fearing an overloading of the organism by extraneous protein. But on the following day, if the case required it, we repeated the injection with the same

or lesser amount. Usually we injected the indicated amount of serum in the mornings over a three consecutive day period. And only in exceptional cases was the serum injected in the morning and in the evening. The following were the indications to discontinue the serum injections: 1) A drop of temperature, 2) An improvement of the general condition, 3) A contraction of the local manifestations. The temperature either fell critically or with a short lysis, and only with an unforeseen complication of some sort, suppurations for the most part, did the temperature remain high for yet some time. Usually the patients withstood these large doses of serum well, only in 2 or 3 cases did we have a minor collapse, with a threadlike pulse in one case; vomiting rarely occurred. The patient very quickly recovered, however, and he was always taken from the table in a satisfactory condition. Serum manifestations occurred, but independently from the amount of serum injected; they were of short duration, sometimes lasting a few hours in all. We used mercurials other than the specific serum. Topically we applied wet dressings of a solution of mercuric chloride, 1:3,000, and potassium permanganate, 1:1,000, and later a salve dressing. One should note that in those cases where the patient had been given some sort of topical treatment at home, which had been accompanied by a trauma of the tissue, such as a cauterization or a collapsing of a vesicle, a noticeable deterioration occurred during the course of the disease.

Conclusions

1. Antianthrax serum is a specifically effective agent against anthrax; it always prevents the transition of a local infection into a general infection and in many cases cures those already having anthracic septicemia.
2. In serious cases it is necessary to employ the specific serum repeatedly and in massive doses (as much as a liter), observing the patients' temperature, local manifestations and general condition.
3. In the cases of medium gravity, it is possible to administer the serum intramuscularly one time or repeatedly in quantities of 80-200 cm³ per administration; in the serious cases it is necessary to inject the serum intravenously and intramuscularly (80-120 cm³ at a time).
4. Large quantities of serum given intravenously (as much as 150 cm³ at a time) are well withstood by the patients, with the condition of proper administration (slow injection in a warmed state).
5. Serum manifestations with the use of large quantities of antianthrax serum are insignificant; they are observed less frequently than with any other serums and should not arouse apprehension.
6. The specific serum against anthrax evidently acts both antitoxically and bactericidally (the quick disappearance of the causative agent from the blood and also the disappearance of toxic manifestations).
7. A topical treatment of the malignant pustule, involving a trauma of the tissue cannot be tolerated, as it is harmful.
8. It is necessary to widely popularize the use of the serum on the periphery, with which it will succeed, undoubtedly, in lowering the death rate from anthrax.

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